

C1
SCHENK, Dale B.
Application No.: 09/724,319
Page 2

PATENT

antibodies bind to an epitope with residues 1-25 of A β . Some monoclonal antibodies bind to an epitope within amino acids 1-5, 5-10, 10-15, 15-20, 25-30, 10-20, 20-30, or 10-25 of A β .

Prophylactic and therapeutic efficacy of antibodies can be tested using the transgenic animal model procedures described in the Examples.

IN THE CLAIMS:

Please cancel claims 84, 87-88, 90-91, 95-96, 98, and 100; amend claim 99; and, add new claims 101-163 as follows.

C2
99. (Amended) The pharmaceutical composition of claim 97, wherein the antibody is designated as 266.

C3
101. (New) A humanized antibody that specifically binds an epitope contained within positions 13-28 of A β .

102. (New) A humanized antibody that binds to soluble A β .

103. (New) A humanized antibody that sequesters A β peptide from its bound, circulating form in the blood, and alters clearance of soluble and bound forms of A β in central nervous system and plasma.

104. (New) The humanized antibody of claims 101, 102, or 103 that is an intact humanized antibody.

105. (New) The humanized antibody of claims 101, 102, or 103 that is a fragment.

106. (New) The humanized antibody of claims 101, 102, or 103 that specifically binds to an epitope having an amino acid between positions 10-20, 10-25, 13-28, 15-20, or 20-30 of A β .

Cont
C3
SCHENK, Dale B.
Application No.: 09/724,319
Page 3

PATENT

107. (New) The humanized antibody of claims 101, 102, or 103 that specifically binds to an epitope within amino acid residues 10-20, 10-25, 13-28, 15-20, or 20-30 of A β .

108. (New) The humanized antibody of claims 102, or 103 that specifically binds to an epitope within amino acid residues 13-28 of A β .

109. (New) The humanized antibody of claims 102, or 103 that specifically binds to an epitope having an amino acid between positions 13-28 of A β .

110. (New) The humanized antibody of claims 101, 102, or 103 that specifically binds to an epitope of A β to which antibody 266 binds.

111. (New) The humanized antibody of claims 102 or 103, which specifically binds an epitope contained in positions 10-20, 13-28, or 15-20 of said A β peptide.

112. (New) The humanized antibody of claim 111, which specifically binds an epitope that includes positions 15-20 of said A β peptide.

113. (New) The humanized antibody of claim 111, which specifically binds an epitope that includes positions 16, 17 or 18 of said A β peptide.

114. (New) The humanized antibody of claims 101, 102, or 103, which is a single chain antibody.

115. (New) The humanized antibody of claims 101, 102, or 103, which comprises human framework regions.

116. (New) The humanized antibody of claims 101, 102, or 103, which comprises CDR.

Cont
C3
SCHENK, Dale B.
Application No.: 09/724,319
Page 4

PATENT

117. (New) The humanized antibody of claims 101, 102, or 103, which is humanized Mab 266.

118. (New) The humanized antibody, or fragment thereof, of claim 117, comprising a humanized light chain comprising the light chain complementarity determining regions (CDRs) from the mouse monoclonal antibody 266 and a light chain variable region framework sequence from a human immunoglobulin light chain; and a humanized heavy chain comprising the heavy chain CDRs from the mouse monoclonal antibody 266 and a heavy chain variable region framework sequence from a human immunoglobulin heavy chain.

119. (New) An antibody fragment obtainable by enzymatic cleavage of the humanized antibody of any one of claims 101-118.

120. (New) The fragment of claim 119 which is an Fab or F(ab')₂ fragment.

121. (New) The fragment of claim 120, which is an F(ab')₂ fragment.

122. (New) The fragment of claim 120, which is an F(ab')₂ fragment.

123. (New) The humanized antibody or fragment of any one of claims 101-122 that is an IgG1 immunoglobulin isotype.

124. (New) The humanized antibody or fragment of any one of claims 101-119, wherein the antibody or fragment thereof is produced in a host cell selected from the group consisting of a myeloma cell and a Chinese hamster ovary cell.

125. (New) The humanized antibody or fragment of any one of claims 101-124, which is administered peripherally to a human subject, to exert its beneficial effects.

126. (New) The humanized antibody or fragment of any one of claims 101-124, which, when administered peripherally to a human subject, does not need to cross the subject's blood-brain barrier to exert its beneficial effects.

SCHENK, Dale B.
Application No.: 09/724,319
Page 5

PATENT

127. (New) The humanized antibody or fragment of any one of claims 101-124, which, when administered peripherally to a human subject, does not require cellular responses in the subject's brain to exert its beneficial effects.

128. (New) The humanized antibody or fragment of any one of claims 101-124, which, when administered peripherally to a human subject, does not substantially bind aggregated A β in the subject's brain.

129. (New) The humanized antibody or fragment of any one of claims 101-124, which, when administered peripherally to a human subject, exhibits beneficial effects without necessarily binding to A β plaques in the brain.

130. (New) A nucleic acid, comprising a sequence coding for the light chain or the heavy chain of the humanized antibody of any one of claims 101-129, or a fragment thereof.

131. (New) One or more nucleic acids, which when expressed in a suitable host cell, yield an antibody of any one of claims 101-129.

132. (New) An expression vector for expressing the antibody or fragment of any one of claims 101-129 comprising nucleotide sequences encoding said antibody or fragment.

133. (New) A cell transfected with the expression vector of claim 132.

134. (New) A cell transfected with two expression vectors of claim 132, wherein a first vector comprises a nucleotide sequence encoding a light chain and a second vector comprises a nucleotide sequence encoding a heavy chain, wherein the first and second nucleotide sequences are components of the vector of claim 132.

135. (New) A recombinant cell that produces the humanized antibody or fragment of any one of claims 117-118.

Cont
C3

SCHENK, Dale B.
Application No.: 09/724,319
Page 6

PATENT

136. (New) The cell of any one of claims 133-135, wherein the cell is selected from the group consisting of a myeloma cell, a Chinese hamster ovary cell and a Syrian hamster ovary cell.

137. (New) A pharmaceutical composition that comprises the humanized antibody or fragment of any one of claims 101-129, and a pharmaceutically acceptable excipient.

138. (New) A method to inhibit the formation of amyloid plaques in humans, comprising administering to a human subject in need or such inhibition an effective amount of a humanized antibody or fragment thereof that specifically immunoreacts with an epitope contained in positions 13-28 of A β .

139. (New) A method to reduce amyloid plaques in humans, comprising administering to a human subject in need of such reduction an effective amount of a humanized antibody or fragment thereof which specifically immunoreacts with an epitope contained in positions 13-28 of A β .

140. (New) A method to inhibit the formation of amyloid plaques in humans, comprising administering to a human subject in need of such inhibition an effective amount of a humanized antibody or fragment thereof that binds to soluble A β peptide.

141. (New) A method to inhibit the formation of amyloid plaques in humans, comprising administering to a human subject in need of such inhibition an effective amount of a humanized antibody or fragment thereof that sequesters A β peptide from its bound, circulating form in blood.

142. (New) A method to reduce amyloid plaques in humans, comprising administering to a human subject in need of such reduction an effective amount of a humanized antibody or fragment thereof which binds to soluble A β peptide.

SCHENK, Dale B.
Application No.: 09/724,319
Page 7

PATENT

Cont
C3
143. (New) A method to reduce amyloid plaques in humans, comprising administering to a human subject in need of such reduction an effective amount of a humanized antibody or fragment thereof which sequesters A β peptide from its bound, circulating form in blood.

144. (New) The method of any of claims 138-143, wherein said antibody or fragment, when administered peripherally to humans, does not need to cross the blood-brain barrier to inhibit the formation of amyloid plaques.

145. (New) The method of claim 138 or claim 139, wherein said antibody or fragment, when administered peripherally to humans, does not elicit cellular responses to inhibit the formation of amyloid plaques.

146. The method of any of claims 138-143, wherein said antibody or fragment, when administered peripherally to humans, does not substantially bind aggregated A β in the brain.

147. (New) The method of any one of claims 138-146, wherein the subject is diagnosed with clinical or pre-clinical Alzheimer's disease or Down's syndrome.

148. (New) The method of any one of claims 138-146, wherein the subject is not diagnosed with clinical or pre-clinical Alzheimer's disease or Down's syndrome.

149. (New) The method of any one of claims 138-139 or 144-148, wherein the antibody is administered by a peripheral route.

150. (New) The method of claim 149, wherein the antibody is administered by an oral, intraperitoneal, subcutaneous, intramuscular, or intravenous route.

Cont
13

SCHENK, Dale B.
Application No.: 09/724,319
Page 8

PATENT

151. (New) A method of reversing cognitive decline in a subject comprising administering to the subject an effective amount of a humanized antibody or fragment of any one of claims 101-129.

152. (New) A method of improving cognition in a subject comprising administering to the subject an effective amount of a humanized antibody or fragment of any one of claims 101-129.

153. (New) A method of treating cognitive decline in a subject comprising administering to the subject an effective amount of a humanized antibody or fragment of any one of claims 101-129.

154. (New) A method of preventing cognitive decline in a subject comprising administering to the subject an effective amount of a humanized antibody or fragment of any one of claims 101-129.

155. (New) The method of any one of claims 151-154, wherein said antibody or fragment is administered peripherally to humans.

156. (New) The method of any one of claims 151-154, wherein said antibody or fragment, when administered peripherally to humans, does not need to cross the blood-brain barrier to affect cognition.

157. (New) The method of any one of claims 151-154, wherein said antibody or fragment, when administered peripherally to humans, does not require cellular responses to affect cognition.

158. (New) The method of any one of claims 151-154, wherein said antibody or fragment, when administered peripherally to humans, does not substantially bind aggregated A β in the brain.